The application has been amended to include an Abstract of the Disclosure.

Claim rejections under 35 USC 112, 2nd paragraph

The Examiner has objected to the terms "disrupting" and "disrupts". Applicants submit that these terms would be clear to one of skill in the art. Indeed these terms are used in a simular context in the three prior art patents cited by the Examiner. However, in order to facilitate the prosecution of this application, these terms have been deleted without prejudice from the claims. The claims, therefore, now refer simply to compounds capable of inhibiting the interaction.

The Examiner has raised a number of objections to the use of the term "TRAM" in the claims. Claim 36 has, therefore, been amended to specify that TRAM is an abbreviation for Transcriptional Adaptor Motif, and that the TRAM in question is selected from the sequences shown in SEQ ID NOs: 3 to 9. Applicants submit that the intended scope of this language is clear and that any polypeptide comprising one of these TRAM motifs would be suitable for use as a first polypeptide in a method of the invention.

The second polypeptide has been further defined as being polypeptide E6 of HPV-16 or HPV-18. The claims therefore refer specifically to the interaction demonstrated in the present application between the motifs of SEQ ID NO's 3 to 9 and sequences within the E6 polypeptides of HPV-16 and HPV-18. Reference to "TRIM" has also been deleted from the claims, leaving a reference to "a sequence which binds to a TRAM sequence".

The Examiner has further objected to the term "determining" in claim 36. Applicants submit that it would be clear to the skilled person that a determination of the ability of a

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candidate compound to inhibit binding between the first and second polypeptides could be carried out in a multitude of ways. The present invention lies in the interaction that takes place between the first and second polypeptide, not in the specific method of determining that is used.

Numerous methods are known in the art for setting up a screening assay based on a protein-protein interaction and these would be achievable by, and known to, one of skill in the art. For example, data is provided in the description of the present application in which a mammalian cell 2-hybrid assay is used with a readable output. Any such assay method for assessing a protein-protein interaction could be used here and Applicants submit that it would be unduly restrictive to require the claims to refer to a specific assay method.

Claims 43, 53 and 56 have been amended to specify that mdm2 comprises a sequence of SEQ ID NO: 6 or 7, that CBP is an abbreviation for CREB binding protein and comprises a sequence of SEQ ID NO: 3, 4 or 5, and that p300 comprises a sequence of SEQ ID NO: 8 or 9. It is believed that these amendments over come the Examiner's rejections.

Claim 54 has been amended to depend upon claim 36 as suggested by the Examiner. Claim 54 has been further amended to replace the term "TRIM sequence" with reference to a sequence which binds a TRAM sequence. Claim 55 has been cancelled.

Reference to "1b" in claim 57 has been corrected to read "100" as suggested by the Examiner. The basis for this correction can be found at page 7, line 25 of the application as filed.

Reconsideration is requested.

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Claim rejections under 35 USC 112, first paragraph

The claims have been amended to refer to an *in vitro* method of identifying compounds that inhibit the interaction of a polypeptide comprising a sequence of one of SEQ ID NOs: 3 to 9 with the E6 protein of either HPV-16 or HPV-18. The Examiner has indicated at page 5 of the instant Action that this subject matter is considered to be enabled. The Examiner's rejection based on an alleged lack of enablement is, therefore, believed to be overcome.

The Examiner has rejected the claims on the basis of an alleged lack of written description. The claims have now been amended to specify the TRAM sequences of SEQ ID NO's 3 to 9 and the E6 proteins of HPV-16 and HPV-18.

The Examiner suggests that the specification only describes sequences "consisting of" SEQ ID NO's 3 to 9. However, although the TRAM sequences themselves "consist" of the sequences of SEQ ID Nos: 3 to 9, it is clear from the application as a whole that the invention relates to polypeptides which comprise such TRAM sequences (see for example page 1, lines 4 and 5, page 3, line 7 and page 3, line 9). For example, at page 3. lines 16 to 22, it is explained that the first polypeptide may be, for example, a polypeptide found in eukaryotic cells, such mdm2, CBP and p300. These are polypeptides which comprise the motifs of SEQ ID NO's 3 to 9. There is no suggestion that the invention is restricted to the use of the motifs *per se* and it is clear from the application as a whole that any polypeptide comprising one of these motifs is suitable for use in the claimed methods.

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Applicants, therefore, submit that molecules within the full scope of the claims have been described and that the specification provides an adequate written description of claimed invention.

Reconsideration is requested.

Rejections under 35 USC 102

The Examiner has rejected claims 36 to 43, 35 to 57 as allegedly being anticipated by Androphy *et al* (US 5,821,051).

The present claims refer to the interaction between polypeptides comprising anyone of SEQ ID NOs: 3 to 9, and the E6 polypeptide of HPV-16 or HPV-18. Androphy *et al* describes the binding of "E6-BP" polypeptides with papilloma virus E6 protein.

The E6-BP polypeptides of Androphy *et al* are specified in SEQ ID NO's 8 to 14 of that patent. None of those sequences includes any of the transcriptional adaptor motifs of SEQ ID NOs: 3 to 9 of the present application. Androphy *et al* does not, therefore, disclose a "TRAM" containing polypeptide as required by the present invention. None of the three specific TRAM-containing polypeptides referred to in the claims of the present application (p300, CBP and mdm2) are mentioned by Androphy.

Further, Androphy *et al* refers generally to any papilloma virus E6 protein, and polypeptides capable of binding any such E6 protein. The Examiner himself has noted at pages 6 to 8 of the instant Action that this field is highly unpredictable and that it would

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involve undue experimentation for one of ordinary skill in the art to determine which protein of HPV in general and which HPV E6 protein in particular to utilize in a method.

Androphy *et al* therefore provides no teaching of a method of the present invention, and in particular provides no suggestion that a polypeptide comprising a TRAM sequence of any of SEQ ID NO s 3 to 9 would be capable of binding to the E6 polypeptide of HPV-16 or HPV-18.

The Examiner further rejects claims 36 to 43, 53 to 57 as allegedly being anticipated by both Chene *et al* (WO 97/11367) and Lane *et al* (WO 98/01467).

Chene *et al* and Lane *et al* both deal with the specific interaction between p53 and mdm2. Neither of these documents teaches or would have suggested that mdm2 might bind to an E6 polypeptide of HPV-16 or HPV-18. Further, the region of mdm2 that is involved in the interaction with p53 has been well defined and does not comprise a sequence of any of SEQ ID NO's 3 to 9. Neither Chene *et al* nor Lane *et al* therefore teach the method of the present invention. In particular, neither of these documents demonstrates or would have suggested an interaction between a polypeptide comprising one of the sequence so of SEQ ID NO's 3 to 9 and the E6 polypeptide of HPV-16 or HPV-18.

Reconsideration is requested.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "Version With Markings To Show Changes Made."

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

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O'CONNOR et al
Serial No. 09/701,080

Respectfully submitted,

NIXON & VANDERHYE, P.C.

By _____
Mary J. Wilson
Reg. No. 32,955

MJW:tat

1100 North Glebe Road, 8th Floor
Arlington, Virginia 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

36. (Twice Amended) A method for determining whether a compound is capable of inhibiting [or disrupting] an interaction between a first polypeptide and a second polypeptide said method comprising:

(a) (i) incubating said first polypeptide with said second polypeptide *in vitro* under conditions which allow the first polypeptide to bind to the second polypeptide to form a complex; and bringing the complex thus formed into contact with a candidate compound; or

(ii) incubating said first polypeptide with said second polypeptide *in vitro* in the presence of a candidate compound under conditions which would allow the first polypeptide to bind to the second polypeptide in the absence of the candidate compound; and

(b) determining if said candidate compound inhibits [or disrupts] binding of the first polypeptide to the second polypeptide;

wherein said first polypeptide comprises a Transcriptional Adaptor Motif (TRAM) [TRAM] sequence [consisting essentially] of any one of the [sequence show] sequences shown in [in] SEQ ID NO:[1] 3 to 9 and said second polypeptide is a human papillomavirus (HPV) polypeptide E6 of HPV-16 or HPV-18 comprising a [TRIM] sequence which binds to a said TRAM sequence.

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43. (Twice Amended) The method according to claim 41 wherein said eukaryotic polypeptide is selected from mdm2 comprising a sequence of SEQ ID NO:6 or 7, CREB binding protein (CBP) comprising a sequence of SEQ ID NO:3, 4 or 5 [CBP], and p300 comprising a sequence of SEQ ID NO:8 or 9.

53. (Amended) The method according to claim 36 wherein the first polypeptide is CREB binding protein (CBP) [CBP] comprising a sequence of SEQ ID NO:3, 4 or 5.

54 (Amended) The method according to claim [52] 36 wherein the [TRIM] sequence which binds said TRAM sequence is located within the second zinc finger of HPV-16 or -18 E6 protein.

56. (Amended) The method according to claim 36 wherein said first polypeptide is p300 comprising a sequence of SEQ ID NO:8 or 9 [and said HPV polypeptide is an E6 polypeptide].

57. (Amended) The method according to claim 36 wherein said second polypeptide comprises the sequence of amino acids 100 [1B] to 147 of SEQ ID NO: 18.

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